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Earlier Detection of Antiphospholipid Syndrome

A Senior Honors Thesis

Submitted in Partial Fulfillment of the Requirements
for Graduation in the Honors College

By
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The College at Brockport
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Earlier Detection of Antiphospholipid Syndrome

Abstract

A 52-year-old man is sitting at home watching a baseball game when all of a sudden the vision in both his eyes went black. He described it as if someone pulled a “Venetian blind” over his eyes. He has a past medical history of aortic stenosis. He was taking Valsartan, Atorvastatin, B-12, Folic Acid, and Vitamin D-3 before the episode. He was prescribed Xarelto after the episode. It was found that he had an optical stroke. Since the pressure in the eye was relieved, partial eyesight returned. He now has full vision in his right eye, but only peripheral vision in his left eye. At first it was believed that the stiffened valve must have thrown the clot and it just traveled to the eye, but since the cardiologist refused to believe that it was his valve the actual cause was discovered, antiphospholipid disorder. It was found that the patient had elevated anti-cardiolipin antibodies that caused the blood clot to form. The patient’s life as a whole is now altered completely due to a preventable thrombotic event. His children also had to be tested because this disease has a genetic component so it is not only him that is affected by this. If this man had been tested earlier for antiphospholipid syndrome then this whole event could have been avoided and his life would be different today.

Antiphospholipid syndrome (APS) is a rare blood clotting disorder that affects about five people in 100,000 per year making it a rare disease (Lopes et al, 2017). The National Heart, Lung, and Blood Institute (n.d.) currently lists the symptoms of antiphospholipid syndrome as deep vein thrombosis, unexplained pregnancy loss, stillbirth, stroke, and in some cases a rash. These symptoms are life-altering and in some cases even fatal. Many times people who have antiphospholipid syndrome have to experience one of these significant events before they are even tested for the clotting disorder. If any of these symptoms are experienced it is advised you

seek emergency medical attention immediately. This lists includes stroke, bleeding, pulmonary embolism, and deep vein thrombosis (“Antiphospholipid Antibody Syndrome | National Heart, Lung, and Blood Institute (NHLBI),” n.d.).

The research question for this thesis is “How can we detect antiphospholipid disorder before it causes a life-altering event like a stroke or a miscarriage?”. This topic is important to the nursing profession because it will condense the many articles available on antiphospholipid syndrome and its signs and symptoms into one main article that a health care professional can refer to for answers on antiphospholipid syndrome. Studying detection of antiphospholipid disorder also has significance in the general community because it will raise awareness and also help to lower the rate of people having life-altering events due to this disease. The aim of this thesis is to provide a singular reference for professionals and the public to access when information on antiphospholipid disorder is needed. In addition to the article there will be a patient teaching brochure to be handed out in doctors’ offices so that the information reaches actual patients.

Background

The role of phospholipids in the blood is to assist in the clotting process. A person with APS creates antibodies that attack the phospholipids in the blood (“Antiphospholipid Antibody Syndrome | National Heart, Lung, and Blood Institute (NHLBI),” n.d.). There are several known risk factors such as autoimmune conditions (systemic lupus erythematosus), certain infections like: syphilis, HIV/AIDS, Hepatitis C, Lyme disease, family history, pregnancy, immobility for extended periods of time, surgery, smoking tobacco, oral contraceptives or estrogen therapy, high cholesterol, and certain medications. There are certain medications that can cause antiphospholipid syndrome, such as hydralazine for high blood pressure, quinidine for heart

dysrhythmias, and phenytoin for seizures, and amoxicillin, which is an antibiotic (“Antiphospholipid Antibody Syndrome | National Heart, Lung, and Blood Institute (NHLBI),” n.d.).

There are many different terms for APS, but many times these different terms cause confusion. One of the different terms for antiphospholipid disorder is lupus anticoagulant, which can give people the impression that only people with systemic lupus erythematosus (SLE) or predominately the people with SLE have APS. This is not the case. About half of antiphospholipid cases are not even associated with rheumatic diseases (Movva, Belilos, & Carsons, n.d.). While the exact prevalence of this disease is hard to determine, around 70% of the people diagnosed with APS are women (“Antiphospholipid Syndrome”, n.d.). Even though the disease is thought to have some genetic link most cases are sporadic, meaning they are present in an individual that has no prior family history of the disease (“Antiphospholipid syndrome”, n.d.).

Cardiac Symptoms

One of the major life-altering complications from APS is myocardial infarction. A myocardial infarction, or heart attack, is defined as blocked blood flow to the heart (“Heart Attack | National Heart, Lung, and Blood Institute (NHLBI),” n.d.). This occurs when the blood clot blocks off a vessel completely and blood can no longer reach a certain part of the heart. Some common symptoms of a myocardial infarction are chest and/or arm pain that is described as pressure, aching, tightening or squeezing that can radiate to the neck, back or jaw, nausea, indigestion, heartburn, abdominal pain, shortness of breath, cold sweat, fatigue, and lightheadedness (“Heart Attack | National Heart, Lung, and Blood Institute (NHLBI),” n.d.). A heart attack can dramatically change the life of the patient.

Heart disease and death from cardiac issues have been linked to abnormalities in aerobic capacity and autonomic nervous system modulation. These abnormalities can be found in patients with autoimmune diseases like systemic lupus erythematosus (SLE), primary antiphospholipid syndrome (PAPS) and rheumatoid arthritis. Garcia et al 's (2013) study looked at PAPS patients' heart rate recovery (HRR) compared to healthy patients' HRR to measure aerobic capacity and cardiac autonomic control (Garcia et al., 2013). The study also found lower VO₂ peak (the amount of work the body produces measured by oxygen usage), time at ventilatory anaerobic threshold (VAT), time-to-exhaustion, and respiratory compensation point (RCP). These findings are consistent with other rheumatologic diseases so this could be an important tool to diagnose or evaluate the risk of PAPS in patients (Garcia et al., 2013).

APS causes multiple cardiac symptoms that can be caught prior to a myocardial infarction, but many physicians do not think to test for it because it is relatively rare ("Antiphospholipid syndrome," n.d.). Increased suspicion of APS is one of the ways to increase detection of this disease. APS has been known to damage a patient's heart valves. One of the valvular diseases linked to APS is Libman-Sacks valvulopathy (Lopes et al., 2017). Libman-Sacks valvulopathy is a form of endocarditis that is not caused by a bacterium. This endocarditis can cause any or all four valves (aortic, pulmonary, bicuspid, and tricuspid) to either develop stenosis, hardening of the valves, or regurgitation, backward flow of blood because of weak valves (Moaref, Afifi, Rezaian, & Rezaian, 2010). Educating providers to investigate the causes of valve issues and endocarditis will help identify APS-related symptoms and make treatment more effective. It is difficult to pinpoint the cause of valvular disease because there are multiple causes so if a patient has multiple risk factors it becomes easy to blame one of the other risk factors and stop investigating.

There are other cardiac symptoms that can lead to the earlier diagnosis of APS. Any kind of blood clot located somewhere in the body could be a symptom of APS and as such should be tested for in anyone with a past medical history of clots. One type of blood clot that happens in the deep veins in one's body, most commonly the legs, is called a deep vein thrombosis. Deep vein thrombosis is not life threatening alone, but they can dislodge from the leg and travel up to the lung where they can be life-threatening. Symptoms of a deep vein thrombosis are pain in the leg, redness or discoloration and a warm feeling in the affected leg ("Venous Thromboembolism | National Heart, Lung, and Blood Institute (NHLBI)," n.d.). A deep vein thrombosis can cause a pulmonary embolism. A pulmonary embolism is caused by the blockage of one of the pulmonary arteries. The symptoms of a pulmonary embolism include shortness of breath, cough, and chest pain ("Venous Thromboembolism | National Heart, Lung, and Blood Institute (NHLBI)," n.d.). Another blood clot is a portal vein thrombosis. A portal vein thrombosis effects the blood supply to the liver and in turn causes the following symptoms: abdominal pain or distention, diarrhea, rectal bleeding, nausea, anorexia, fever, lactic acidosis, splenomegaly, and sepsis (Ponziani et al., 2010).

Neurologic Symptoms

Another life-threatening symptom of having APS is cerebrovascular infarction (stroke) or cerebrovascular accident (CVA). A stroke occurs when the blood supply to the brain is either interrupted or stopped depriving the brain of oxygen and nutrients ("NINDS Know Stroke Campaign - Know Stroke Brochure," n.d.). The strokes seen from antiphospholipid syndrome usually occurs in young adults with no prior history of cardiovascular risk factors (Lopes et al., 2017).

There are other neurologic symptoms that are not life-threatening that can lead to the diagnosis of APS. Some non-critical neurological symptoms of antiphospholipid syndrome are migraine, convulsions, and longitudinal myelitis (Lopes et al., 2017). There are three autonomic nervous system disorders that have been linked to APS that have both cardiac symptoms and neurological symptoms. They include postural orthostatic tachycardia (POTS), neurocardiogenic syncope (NCS) and neurogenic orthostatic hypotension (OH). Postural orthostatic tachycardia manifests as dizziness, syncope, nausea, vomiting, headache, mental clouding, tremulousness, palpitations, chest pain, shortness of breath, and orthostatic hypotension. Postural orthostatic tachycardia occurs mostly in women of reproductive age. The symptoms of neurocardiogenic syncope are low blood pressure, low heart rate, pallor, diaphoresis (sweating), nausea, abdominal discomfort, yawning, and hyperventilation. Neurogenic orthostatic hypotension is caused by an inability to properly vasoconstrict and/or the major fall in cardiac output (Schofield, Blitshteyn, Shoenfeld, & Hughes, 2014).

There have been two studies that looked at cerebrovascular events in the young adult population. Both articles consider a young adult to be someone who is younger than fifty when the thrombolytic event occurred. These studies were created to look at the difference antiphospholipid syndrome can have on your likelihood to have a cerebrovascular event. Patients with APS were found to be five times more likely to have a cerebrovascular event than their unaffected counterparts. Anticardiolipin antibody was also the most frequently detected antibody in the patients experiencing thrombolytic events with a rate of 22% of young stroke patients having it (Sciascia et al., 2015). Sciascia et al. (2015) concluded that including antiphospholipid testing would not only improve the management of APS, but also the diagnosis. More awareness and knowledge needs to be spread about APS to help prevent or to help improve

the prognosis of these patients. There was also a finding that anticardiolipin antibody (aCL) was associated with higher stroke or TIA rates in women and not in men (Mishra & Rohatgi, 2019).

Obstetric Symptoms

Women tend to be effected by antiphospholipid syndrome more than men do (“Antiphospholipid syndrome,” n.d.). This disease can affect women’s ability to bare healthy children. APS can be linked to infertility and pregnancy complications. Some obstetric symptoms of antiphospholipid syndrome are miscarriage or stillbirth, severe preeclampsia, unexplained fetal growth restriction, and chorea Gravidarum (Kochenour, Branch, Rote, & Scott, 1987). Fischer-Betz, Specker, Brinks and Schneider’s (2018) study followed 24 pregnancies in 20 women who had been diagnosed with a CVA due to APS from beginning to end. One pregnancy was lost very early at four weeks and was excluded from the study. Out of the 23 remaining pregnancies two of them resulted in fetal death and eight mothers suffered from preeclampsia. It was found that the mothers that tested positive for multiple antiphospholipid antibodies were at an increased risk for preeclampsia. Four of the pregnancies had an abnormal second trimester Doppler ultrasound result and two of those were the aforementioned fetal demises (Fischer-Betz, Specker, Brinks, & Schneider, 2012). This study found that there is also a higher rate of preterm delivery in mothers with antiphospholipid syndrome with the rate being 26% compared to 4.7% and 19% in the controls (Fischer-Betz, Specker, Brinks, & Schneider, 2012). Earlier investigation into the cause of fetal demise may help prevent additional miscarriages and stillbirths.

Symptoms of Other Body Systems

There are some other body systems that are affected by APS. One of them is the integumentary system or the skin. Some cutaneous expressions of antiphospholipid are

cutaneous gangrene, necrosis of digits, livedo reticularis, lesions resembling vasculitis (nodules & macules), skin ulcerations, and thrombophlebitis (Asherson & Cervera, 1993). Sheth and Parke (2016) presented a case study that followed a woman that developed cutaneous vasculitis secondary to APS. The case study was done on a 52-year-old woman with a significant past medical history of APS and HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome during pregnancy. The day after her wellness visit at the rheumatologist the patient was admitted to the ED with her chief complaint being an erythematous lesion on her chin, which quickly progressed into a dark red plaque. Her vitals were stable and her lab work was within normal limits in the ED, but her physical exam revealed a small area of necrotic tissue and surrounding redness on her chin. A biopsy was performed and the results showed that the patient was experiencing acute vasculitis. She was started on 60 mg prednisone and her symptoms alleviated. A symptom of livedo reticularis is a mottled pattern that is a purple lace-like discoloration caused by the swelling of blood vessels. This usually appears on the trunk, arms or legs and is not relieved by warming (Sheth & Parke, 2016).

Another body system that is affected by APS is the immune system. In patients with APS it has been discovered that they are lacking an immunoregulatory cytokine called TGF- B_1 . This immunoregulatory cytokine is responsible for maintaining tolerance by limiting response to self-antigens (Jakiela et al., 2016). In people who have a deficiency in the TGF- B_1 immunoregulatory cytokine they have enhanced activation of effector T-cells and this leads to severe autoimmunity. It was even found that the higher the antiphospholipid (aPL) titers the more likely they are to have this reaction. These patients do not display symptoms of having an autoimmune disorder, which makes them harder to diagnose. (Jakiela et al., 2016) Overall, the findings of the study found that the immunoregulatory cytokine network plays an important role

in the development of not only diseases like systemic lupus erythematosus (SLE) but also in primary antiphospholipid syndrome (PAP). (Jakiela et al., 2016)

The blood can also be affected by APS. Thrombocytopenia can be caused by APS. Thrombocytopenia is a decreased number of platelets in the blood (“Antiphospholipid syndrome”, n.d.). People with APS can also present as anemic, a shortage of red blood cells, which is caused by the destruction of red blood cells or hemolysis (“Antiphospholipid syndrome”, n.d.). Some other hematologic disease that can be caused by APS are thrombotic thrombocytopenia purpura, sickle cell disease, polycythemia vera, myelofibrosis, Monoclonal gammopathies, and Von Willebrand’s disease (Asherson & Cervera, 1993). Thrombotic Thrombocytopenia Purpura (TTP) can be characterized by fever, confusion, dark or bloody urine, difficulty speaking, seizures, thrombocytopenia, weakness, and hemolytic anemia (Lewis, Bucher, Heitkemper, & Harding, 2017).

The digestive system can also be affected by APS. A case study was written on an individual that had multiple blood clots that had affected his gastrointestinal tract. He presented to the ED complaining of abdominal pain, constipation, nausea, vomiting, and fatigue all lasting over a month. Upon examination the patient looked frail and showed signs of weight loss. He was treated for an obstruction and the symptoms seemed to subside besides the abdominal pain. The patient had a past medical history of end-to-end anastomosis of the small intestine for infarction and gangrene of two-thirds of the intestine. The gangrene was thought to be caused by a blood clot in the mesenteric vein. The abdominal pain was investigated further with an abdominal computed tomography scan. The scan found that there was a venous thrombosis in the inferior vena cava causing Budd-Chiari syndrome. The patient returned two months later complaining of persistent abdominal pain, but this time there was distention that was present for

2 weeks. The patient had lost a considerable amount of weight, pale conjunctivae without jaundice, ascites, mild pitting edema and splenomegaly (“The antiphospholipid antibody syndrome: a case report,” n.d.). The patient continued to have blood-clotting episodes over the next few years until he became septic with a gangrenous scrotum. This patient was showing signs of a coagulation defect for approximately 6 years without further investigation. If the doctors had suspected APS sooner this patient could have been spared years of agony and potential complications. Diagnosing and treating APS can be costly to the patient so doctors are reluctant to run the tests if they don’t see good cause to (“The antiphospholipid antibody syndrome: a case report,” n.d.)

Education

A reoccurring theme in the research on APS is that early detection yields better outcomes for patients and early detection can only happen if providers have a heightened awareness that APS should be tested for. Better education for providers and patients of will help. Patients and their families are generally overwhelmed with anxiety when they are in the hospital so they do not absorb or fully understand the information given to them so follow up education is very important. That is why it is important for staff to identify education programs that are effective, culturally sensitive, and accurate for the problem the patient is facing (DeMarco & Nystrom, 2009). There have been a few studies done to examine preferred method of teaching amongst patients. One study looked at the pros and cons of each teaching method so providers can pick the one they think fits their patient the best. This study looked at traditional lectures, computer technology, written material, discussions, and simulated games as methods of education. It was found that more patients were satisfied with computer-based learning, but there were concerns for retention over time with this method. Computer-based learning was also the preferred method

for children and adolescents showing an immediate knowledge increase (Friedman, Cosby, Boyko, Hatton-Bauer, & Turnbull, 2010). Written information ranked high in patient satisfaction and information recall, but writing every patient an individual letter would create a lot of work for a busy physician. Also written material needs to be at the reading level of the general population. Booklets and informational packets helped to reduce the confusion patients were feeling and improved knowledge, especially if the information was provided before the first appointment (Friedman, Cosby, Boyko, Hatton-Bauer, & Turnbull, 2010). Another study found that lectures and small group work was the most popular teaching method because it incorporated more than one teaching and/or learning methods into one teaching opportunity (Häggman-Laitila, Mattila, & Melender, 2016). It is recommended that patients receive a lay version of their care plan because this enables them to better understand the plan of care. A lay version explains the goals of treatment, different treatment options and benefits and risks of each option. Patients that have access to this are able to become active members of their treatment team and are better equipped for consultations with their health care provider (Schipper, Bakker, De Wit, Ket, & Abma, 2016). Education while the patient is in the hospital is very important, but it does not stop there. Patients need to have continuous education.

Patients with chronic diseases like antiphospholipid syndrome need to have continuous education in an outpatient setting while they learn to live with their disease. A clinic in Singapore has adopted an interesting plan for education in outpatient clinic settings. It is called the Plan-Do-Study-Act cycle. The cycle consisted of four interventions: development of health education slides, organization of a computer station and education materials, initiating an electronic appointment system for educational purposes and training for the staff on patient education materials to support self-care (Heng, Tham, Yoke Eng, Ling, & Menon, 2013).

Intervention one: development of health education slides consisted of developing a series of closely monitored and evaluated series of patient education slides. Intervention two: organization of a computer station and education materials suggest using shelving and other unused equipment in closed wards to display the health education that has been created. Intervention three: initiating an electronic appointment system for education purposes said that since the hospital already had Google applications for email they explored the appointment calendar feature with the help of the IT department. This did not cost the hospital any extra to implement. The last intervention, training for the staff on patient education materials to support self-care was achieved by sessions on patient education material with the Nurse Clinician (Heng, Tham, Yoke Eng, Ling, & Menon, 2013). Patients felt that the designated station for education was helpful, the electronic appointment calendar was easy to use and the training on education materials was clear and easy to understand. It is important for patients and family members to be comfortable using the educational materials because when they learn about their disease or loved one's disease it helps them develop skills, build confidence and reduce any anxiety they are feeling (Heng, Tham, Yoke Eng, Ling, & Menon, 2013).

Conclusion

Earlier detection of antiphospholipid syndrome is important to limit the adverse effects of the disease. Since most patients currently are not diagnosed until after they have a life-threatening event, like a stroke or heart attack, many of them end up with disabilities related to that event. There are earlier symptoms of antiphospholipid syndrome that often go undiagnosed because they are either contributed to some other comorbidity or the cause is not investigated further. Antiphospholipid syndrome can affect multiple different body systems mostly the cardiac, neurological, and reproductive system. People who should be monitored for

antiphospholipid syndrome are people with a family history, any history of thrombotic events, and obstetric complications without a previous explanation.

If a patient is experiencing any of the following symptoms they should be tested for antiphospholipid syndrome: depressed aerobic capacity, autonomic nervous system modulation, damaged heart valves, Libman-Sacks valvulopathy, any blood clot or migraine, convulsions, longitudinal myelitis, postural orthostatic tachycardia (POTS), neurocardiogenic syncope (NCS) and neurogenic orthostatic hypotension (OH), miscarriage or stillbirth, severe preeclampsia, unexplained fetal growth restriction, chorea Gravidarum, cutaneous gangrene, necrosis of digits, livedo reticularis, lesions resembling vasculitis (nodules & macules), skin ulcerations, thrombophlebitis, thrombocytopenia, thrombotic thrombocytopenia purpura, sickle cell disease, polycythemia vera, myelofibrosis, Monoclonal gammopathies, and Von Willebrand's disease. Heightened suspicion of antiphospholipid syndrome is the key to catching it before it causes a life-changing event. Even though antiphospholipid syndrome is considered a rare disease, early diagnosis and treatment for patients with APS is crucial for quality of life and/or survival.

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What is Antiphospholipid Syndrome?

Antiphospholipid syndrome (APS) is a rare blood clotting disorder that affects about 5 people in 100,000 per year making it a rare disease. A person with antiphospholipid syndrome creates antibodies that attack the phospholipids in the blood. It can cause blood clots to happen in people who are affected by this syndrome.¹

If you have more questions or concerns you can go to:

- Mayo Clinic: Antiphospholipid Syndrome
- Medscape.com and search antiphospholipid syndrome
- Genetic Home Reference and search antiphospholipid syndrome



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⁶ 10 Patient Teaching Strategies for Nurses. (n.d.). Retrieved December 7, 2018, from http://lippincottolutions.lww.com/blog_entry.html/2015/03/05/10_patient_teaching-Hs1L.html Photo on back panel

⁷ Doctors Wish List for Health Care Reform | Docs 4 Patient Care Foundation. (n.d.). Retrieved December 7, 2018, from <https://d4pcfoundation.org/doctors-wish-list-for-health-care-reform/> Photo on top left

⁸ Patient Care & Safety | Patients and Visitors | St. Mary's Medical Center. (n.d.). Retrieved December 7, 2018, from <https://www.st-marys.org/patients-and-visitors/patient-care-safety/> photo on bottom inside

Antiphospholipid Syndrome (APS)



Earlier Detection Better Prognosis



Michaela Maertz

The information in this brochure is valid as of December 3, 2018



Early Symptoms of Antiphospholipid Syndrome

Cardiac Symptoms

- Damaged heart valves
- Libman-Sacks valvulopathy
- Blood clots anywhere in the body and other symptoms⁴

Obstetric Symptoms

- Miscarriage or stillbirth
- Severe preeclampsia
- Unexplained fetal growth restriction
- Chorea Gravidarum
- Landry-Guillain-Barré-Strohl syndrome (LGBSS)³

Neurologic Symptoms

- Migraine
- Convulsions
- Longitudinal myelitis and other symptoms¹

Integumentary Symptoms

- Death of the skin from lack of blood flow
- Blackening of the fingers
- Skin lesions and other symptoms²

Hematologic Symptoms

- Inflammation and pain caused by a blood clot
- Low platelet count
- Sickle cell disease
- Polycythemia vera
- Myelofibrosis
- Monoclonal gammopathies
- Von Willebrand's disease²

Q&A

What are the risk factors of antiphospholipid syndrome?

Family history, autoimmune conditions (systemic lupus erythematosus), certain infections like: syphilis, HIV/AIDS, Hepatitis C, Lyme disease, pregnancy, immobility for extended periods of time, surgery, smoking tobacco, oral contraceptives or estrogen therapy, high cholesterol, and certain medications (hydralazine for high blood pressure, quinidine for heart dysrhythmias, and phenytoin for seizures, and amoxicillin, which is an antibiotic).¹

How do you treat APS?

There is no treatment for APS, but patients will be put on an anticoagulant so that they will not develop blood clots.¹

Who does APS usually affect?

While the exact prevalence of this disease is hard to determine, around 70% of the people diagnosed with APS are women. Also, if there is a family history their children are at risk for the disease.¹